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Lipid nanocarriers: Potential for pulmonary delivery

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Lipid nanoparticles are extensively explored colloidal systems as a potential vehicle for site specific delivery of drugs to different organs or systems such as lung, brain, skin and lymphatic etc. Lipid nanoparticles such as solid lipid nanoparticles, nanostructured lipid carriers, liposomes etc. can help in improving efficacy while lowering toxicities of actives. Cellular uptake of drugs can also be enhanced by using lipid nanocarriers. Pulmonary route of delivery is an alternative non-invasive approach for both local and systemic delivery of therapeutic agents. Formulation of drug into inhalable form with sufficient stability and aerodynamic properties are the key challenges associated with the development of pulmonary drug delivery system. In course of our last few years endeavor to deliver drug loaded lipid nanocarriers for the treatment of local lung disorders, we have come up with efficient systems such as proliposomal dry powder for inhalation and nanostructured lipid carrier dry powder for inhalation. We have explored different approaches for the development of the lipid nanocarrier's inhalation system. In one approach, we have developed proliposomes using single step spray drying method and in other we employed lyophilization technique for the successful development of powders for inhalation with desirable aerodynamic properties. Our studies demonstrate encapsulation of drugs such as rifapentine, montelukast, rosuvastatin etc. in lipid nanocarriers modifies the physicochemical as well as in-vivo pharmacokinetic properties. Pulmokinetic parameters such as C_{max}, T_{max}, AUC₀₋₂₄, KE, MRT and t_{1/2} were improved as compared to pure drug. An interesting finding was increased IC₅₀ value of the encapsulated drug, thus reduced in-vitro cytotoxicity in pulmonary cells as compared to the conventional system. Our focus is on application of Quality by Design (QbD) principles for the development of inhalation delivery systems so as to comply with the current regulatory demand. Thus, our group is the first to report the successful application of QbD principles with design of experiment for the efficient development of proliposomal system for inhalation. The talk will highlight the findings of our research.

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The progress of our understanding of pulmonary vascular disease and treatment options

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Pulmonary vascular disease (PVD) is a progressive and potentially fatal disease. Our understanding of PVD has significantly improved over the last 2 decades. This understanding of the different pathophysiologic pathways that lead to PVD has led to the successful development of multiple effective therapeutic interventions. Although this is in general an incurable disease, these therapies are able to control the disease, improve quality of life, and potentially prolong survival. Not all pulmonary vascular diseases are the same. The above mentioned therapies are effective for only one sub-group of pulmonary hypertension (PH): The one classified by the World Health Organization as WHO group 1 PH. This WHO classification of PH is not perfect and there is a lot of overlap in the clinical and pathophysiologic features of the different groups, however it is this classification that facilitated research trials enrollment that lead to effective therapeutics. Better phenotyping of PVD is much needed. The 3 successfully targeted pathways in pulmonary vascular disease in WHO group 1 PH are the Nitric Oxide, Endothelin-1, and prostanoid pathways. The primary effect of the approved drugs targeting these different pathways is vasodilation, although many of them have supplementary but secondary potential effects, such as anti-platelets and/or anti-inflammatory effects. Drugs targeting the primary pathologic processes in WHO group 1 PH are still lacking, and that's a major reason why a cure has not been identified yet. In summary, although progress has been made, we still have ways to go to better understand and treat pulmonary vascular disease.

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